

Hotspots of aberrant epigenomic reprogramming in human induced pluripotent stem cells.

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Public Summary:

Induced pluripotent stem cells (iPSCs) offer immense potential for regenerative medicine and studies of disease and development. Somatic cell reprogramming involves epigenomic reconfiguration, conferring iPSCs with characteristics similar to embryonic stem (ES) cells. However, it remains unknown how complete the reestablishment of ES-cell-like DNA methylation patterns is throughout the genome. Here we report the first whole-genome profiles of DNA methylation at single-base resolution in five human iPSC lines, along with methylomes of ES cells, somatic cells, and differentiated iPSCs and ES cells. iPSCs show significant reprogramming variability, including somatic memory and aberrant reprogramming of DNA methylation. iPSCs share megabase-scale differentially methylated regions proximal to centromeres and telomeres that display incomplete reprogramming of non-CG methylation, and differences in CG methylation and histone modifications. Lastly, differentiation of iPSCs into trophoblast cells revealed that errors in reprogramming CG methylation are transmitted at a high frequency, providing an iPSC reprogramming signature that is maintained after differentiation.

Scientific Abstract:

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